

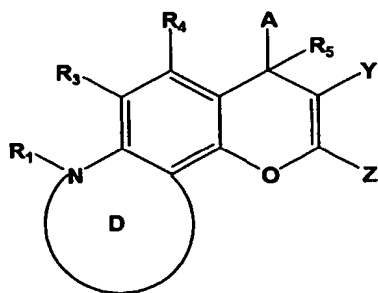
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
27 November 2003 (27.11.2003)

PCT

(10) International Publication Number
WO 03/097806 A2

- (51) International Patent Classification⁷: **C12N** [CA/CA]; 12670 52e Avenue, Montreal, Québec H1E 2H5 (CA).
- (21) International Application Number: PCT/US03/15427
- (22) International Filing Date: 16 May 2003 (16.05.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/378,079 16 May 2002 (16.05.2002) US
- (71) Applicants (for all designated States except US): **CYTOVIA, INC.** [US/US]; 6650 Nancy Ridge Drive, San Diego, CA 92121 (US). **SHIRE BIOCHEM, INC.** [CA/CA]; 275 Armand-Frappier Boulevard, Laval, Québec H7V 4A7 (CA).
- (72) Inventors; and
- (73) Inventors/Applicants (for US only): **CAI, Sui Xiong** [US/US]; 3623 Berryfield Court, San Diego, CA 92130 (US). **JIANG, Songchun** [US/US]; 10512 Rancho Carmel Drive, San Diego, CA 92128 (US). **KEMNITZER, William, E.** [US/US]; 2838 Bay Canyon Court, San Diego, CA 92117 (US). **ZHANG, Hong** [CN/US]; 5139 Clairemont Mesa Boulevard, Apartment 110, San Diego, CA 92117 (US). **ATTARDO, Giorgio** [CA/CA]; 2740 Prudentiel, Laval, Québec H7K 3M1 (CA). **DENIS, Real**
- (74) Agents: **ESMOND, ROBERT W.** et al.; Sterne, Kessler, Goldstein & Fox, P.L.L.C., 1100 New York Avenue, Washington, DC 20005 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published: — without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED 4-ARYL-4H-PYRROLO[2,3-H]CHROMENES AND ANALOGS AS ACTIVATORS OF CASPASES AND INDUCERS OF APOPTOSIS AND THE USE THEREOF

(I)

(57) Abstract: The present invention is directed to substituted 4H-chromenes and analogs thereof, represented by the Formula (I): wherein R¹, R³, R⁵, A, D, Y and Z are defined herein. The present invention also relates to the discovery that compounds having Formula (I) are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clinical conditions in which uncontrolled growth and spread of abnormal cells occurs.